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TITLE: Evaluation of Neurophysiologic and Systematic Changes during Aeromedical Evacuation and en Route Care of Combat Casualties in a Swine Polytrauma

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14. ABSTRACT There is a dearth of knowledge about the effects of long range aero-medical evacuation on injured organs, as well as an emerging published database suggesting clinically significant adverse effects of hypobaria on even healthy tissues. Cabin pressure is equivalent to an altitude around 8,000ft. at which inspired oxygen is sufficient to maintain blood oxygen saturation above 90% in a healthy individual. In combat casualties with multiple injuries this could however compromise oxygen delivery and result in hypoxemia. Additionally, increase in altitude with concomitant decrease in atmospheric pressure allows gas expansion in body cavities. The volume of trapped gas expands by approximately 35% from sea level to an altitude of 8,000 feet. This can expose already vulnerable patients to severe complications. In light of this, a thorough investigation of the effects of hypobaria in clinical settings simulating the most important injury patterns encountered by combat casualties is necessary to optimize treatment efficacy and safety. During the second year of this project, pilot experiments to test the hypobaric chamber in a live, anesthetized animal have been completed. Unexpected issues with animal temperature control, anesthesia delivery, and Total Intravenous anesthesia have been resolved. Animals experiment under normobaric and hypobaric conditions have been initiated. The NMRC Center for Hypobaric Experimentation, Simulation and Testing (CHEST) provides a unique platform for evaluation of long-range evacuation effects on physiology and therapeutic interventions in military relevant large animal combat injury models, which may contribute to optimization of combat casualty care and evacuation guidelines.					
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## Table of Contents

	<u>Page</u>
Introduction.....	3
Body.....	3-5
Key Research Accomplishments.....	5
Reportable Outcomes.....	5
Conclusion.....	5
References.....	5
Appendices.....	5
Supporting Data.....	6-8

## INTRODUCTION:

Rapid evacuation of combat casualties to definitive care in the United States is practice based on evidence derived from recent military conflicts and has greatly diminished morbidity and mortality among combat casualties. However, not much is known about the effects of long range aero-medical evacuation in hypobaric environments on the physiology and organ function of injured warfighters, thus potentially and unknowingly putting combat casualties at risk during evacuation. Traumatic brain injury (TBI) patients are of particular concern, since small changes in ambient conditions such as cabin pressure and temperature could potentially have detrimental effects on the already vulnerable brain. There is evidence that hypobaria as well as in-flight cabin pressure fluctuations can induce neurological symptoms in otherwise healthy persons due to altitude decompression sickness. This suggests that high altitude hypobaric conditions can have detrimental effects on pulmonary and neurologic outcome and that aero-medical conditions and/or therapeutics can be optimized to attenuate such adverse effects.

Our hypothesis is that hypobaria during simulated long-range aero-medical evacuation has adverse effects on brain blood flow and tissue oxygenation, as well as lung function in swine models of neurotrauma and polytrauma. We plan to investigate the effects of aero-medical evacuation on neurophysiology and lung function in swine models of TBI with and without hemorrhagic shock (HS) and/or ARDS (polytrauma).

## BODY:

Tasks 1 (build hypobaric chamber) and 2 (secure IACUC approval) have been completed in Year 1 of this grant. The following two tasks were scheduled to be continued within the second year of this grant:

### **Task 3. Animal experiments during normobaric conditions (months 5-28):**

*Subtask 1. Complete 72 animal experiments in Sham, TBI alone, TBI+HS, ARDS alone, TBI+ARDS and TBI+HS+ARDS groups. Animals will be randomized (months 5-28)*

*Subtask 2. Hematologic and hematologic analysis of blood samples (months 5-28).*

*Subtask 3. Necropsy, gross pathology, histopathologic analysis (months 5-28).*

Animal experiments have been initiated under normobaric conditions and continue as scheduled.

### **Task 4. Animal experiments during hypobaric conditions (months 15-39):**

*Subtask 1. Complete 10 pilot animals to test hypobaric chamber and animal set up for monitoring within the chamber (months 15-16).*

*Subtask 2. Complete 72 animal experiments in Sham, TBI alone, TBI+HS, ARDS alone, TBI+ARDS and TBI+HS+ARDS groups. Animals will be randomized (months 17-39)*

*Subtask 3. Hematologic and hematologic analysis of blood samples (months 17-39).*

*Subtask 4. Necropsy, gross pathology, histopathologic analysis (months 17-39).*

Pilot studies have been completed.

During the first complete experiments it was noted that it is very challenging to control the animal's temperature with the current set-up (circulating water mat). We identified brushless fans that can be used in the hypobaric chamber set up. We also noted that it is necessary to procure intravenous infusion pumps with power back up to avoid an interruption of anesthetic flow when the animal is moved from the operating room to the hypobaric chamber room.

Animal experiments were put on hold until temperature and anesthesia control measures were in place. Brushless fans have been installed in the hypobaric chamber and battery powered intravenous fluid infusion pumps have been received. Animals experiments have been resumed. Animal temperature control and continuous anesthesia delivery has been achieved.

The transition from inhalation anesthesia to total intravenous anesthesia (TIVA) has not been optimal as evidenced by unexpected physiologic instabilities in control animals. We were able to optimize drug concentrations and added intramuscular midazolam to the anesthesia induction cocktail. This resulted in stable conditions during control experiments as seen in Figures 1 and 2.

Animal experiments for sham and ARDS groups have been initiated.

#### **KEY RESEARCH ACCOMPLISHMENTS:**

- Complete pilot experiments to test chamber in a live, anesthetized animal.
- Resolved unexpected issues with animal temperature control, anesthesia delivery, and TIVA
- Initiated animal experiments under normobaric and hypobaric conditions.

#### **REPORTABLE OUTCOMES:**

None.

#### **CONCLUSION:**

The hypobaric chamber for simulating swine experiment during long-range aeromedical evacuation flights built for this grant provides a unique platform for evaluation of long-range evacuation effects on physiology and therapeutic interventions in military relevant large animal combat injury models. The creation of the NMRC Center for Hypobaric Experimentation, Simulation and Testing (CHEST) may contribute to optimization of combat casualty care and evacuation guidelines.

#### **REFERENCES:**

None.

#### **APPENDICES:**

None.

## SUPPORTING DATA:

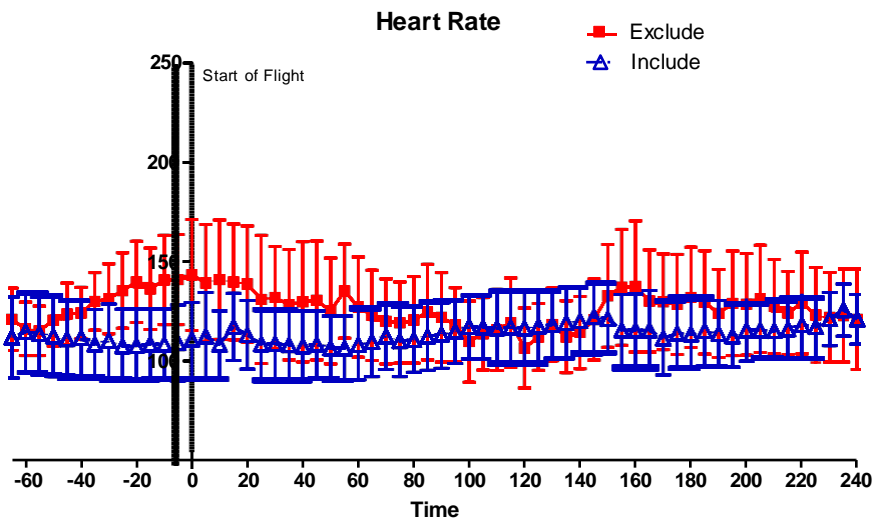


Figure 1: Heart rate in the excluded animals was very unstable before the flight (transition from inhalation to IV anesthesia, and then even during the flight). Included animals are control animals that benefited from anesthesia optimization and demonstrate stable hear rate throughout the experiment.

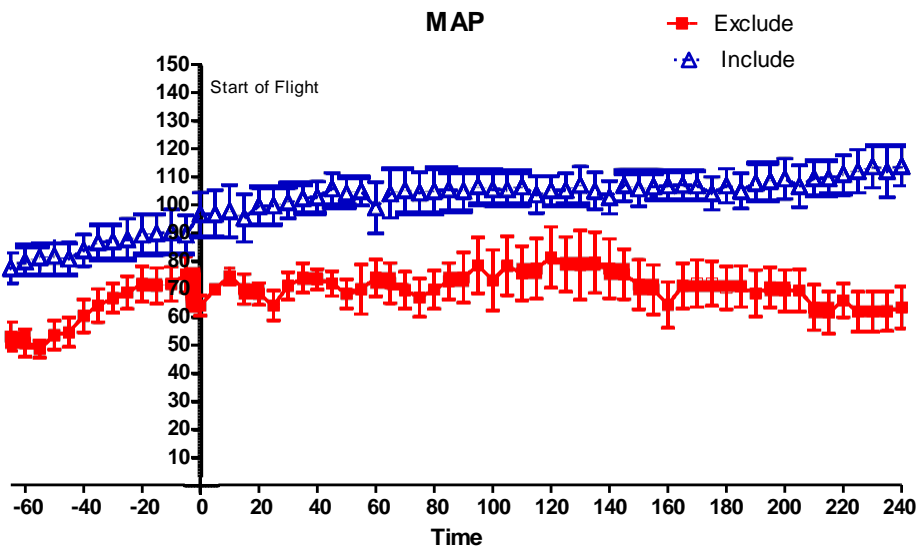


Figure 2: Mean arterial blood pressure (MAP) in the excluded animals was very unstable before the flight and during the flight. It was also uncharacteristically low, indicating confounding conditions. Included animals are control animals that benefited from anesthesia optimization and demonstrate stable steady MAP throughout the experiment.

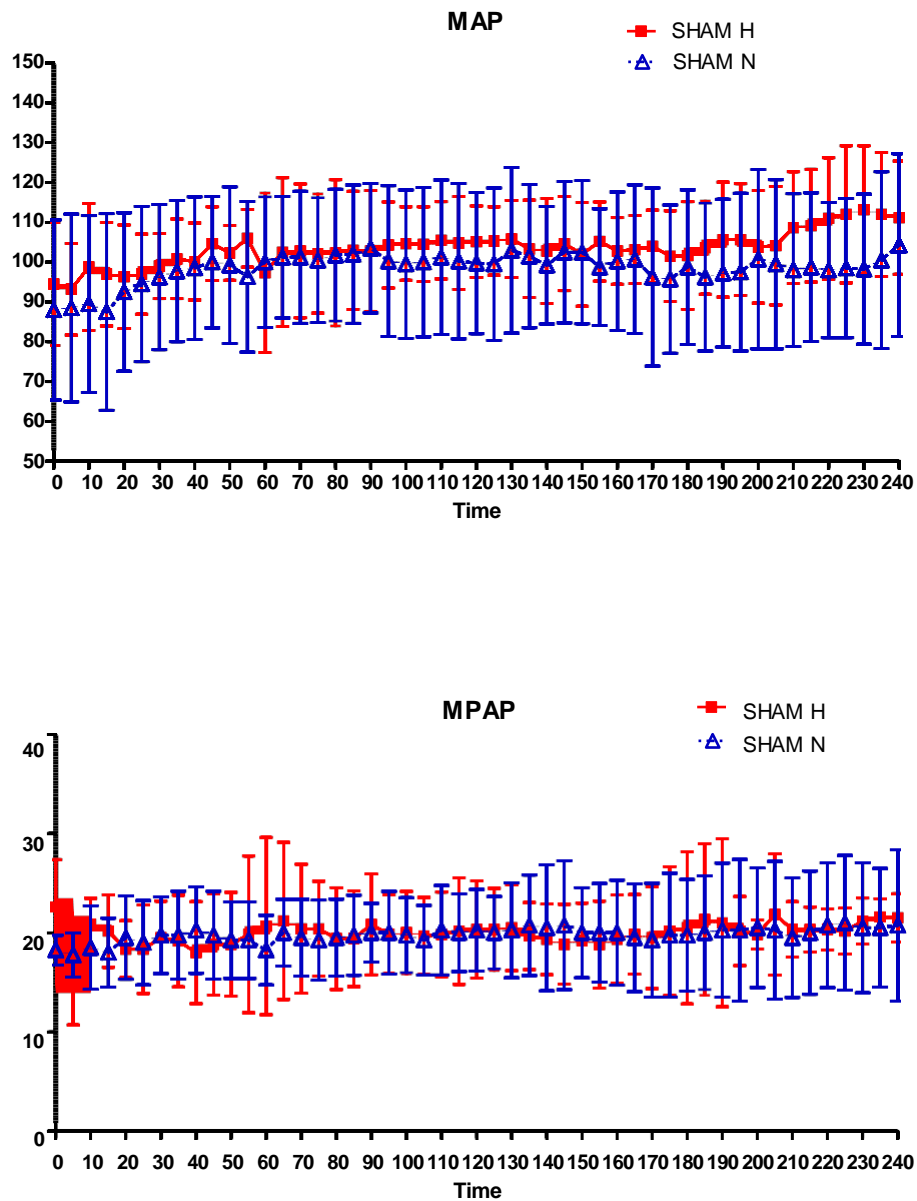


Figure 3 and 4: Mean Systemic (MAP) and Pulmonary (MPAP) Artery pressures demonstrate stable conditions in both normobaric and hypobaric control animals. This illustrates the reproducibility and stability of the model.

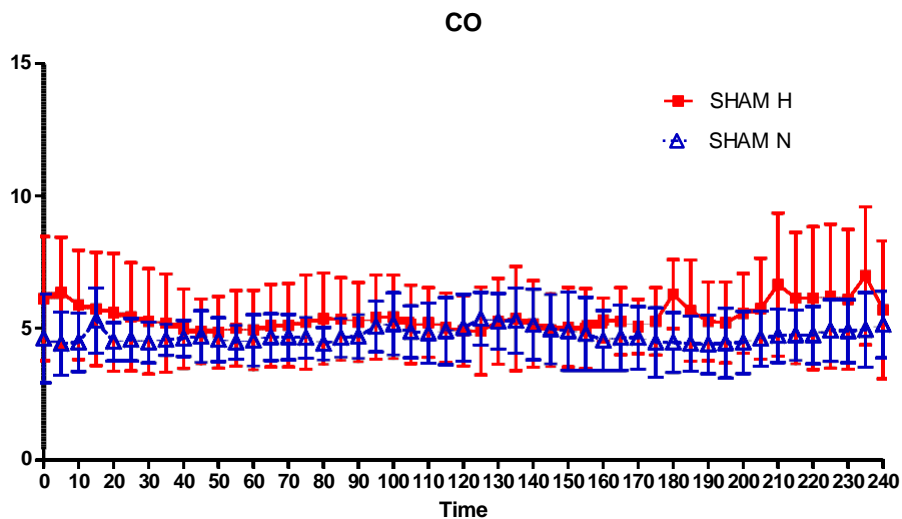


Figure 5: Towards the last third of the 4 hour flight, Cardiac Output (CO) in the hypobaric animals tended to increase compared to the normobaric controls.

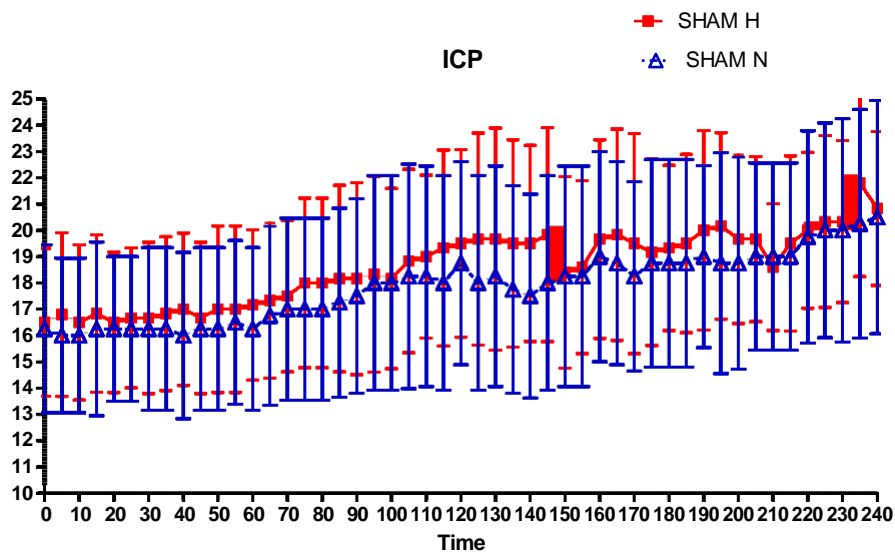


Figure 6: Intracranial Pressure (ICP) showed mild increase during the second half of the flight in both groups. Large variation and low sample size at this point of the study prevent adequate interpretation of this finding.